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HUMAN PERFORMANCE FOLLOWING ANTIHISTAMINE ADMINISTRATION

NMRI 90-127

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The objective of this research was to evaluate the effects of two antihistamines on a range of cognitive performances. Diphenhydramine was chosen because of its purported central nervous system effects, while terfenadine was chosen because of its purported lack of similar effects. Six male subjects were trained on the nine task Naval Medical Research Institute Performance Assessment Battery (NMRIPAB) until performance accuracy was at least 90% for three consecutive sessions. They were subsequently administered either 60 mg of terfenadine, 100 mg of diphenhydramine, or placebo in a mixed order. Each condition was replicated three times. NMRIPAB sessions were conducted 1 hour, 2 hours, and 3 hours

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19. post drug administration. Diphenhydramine produced selective decreases in the accuracy of responding on five of the nine NMRIPAB tasks. It also produced increases in response latency in two of the nine tasks. The majority of diphenhydramine effects occurred during the second or third hour of testing, which is in conformance with the reported pharmacokinetics of the compound. Terfenadine did not produce consistent effects on any task. Each subject exhibited differing patterns of task sensitivity to diphenhydramine administration.

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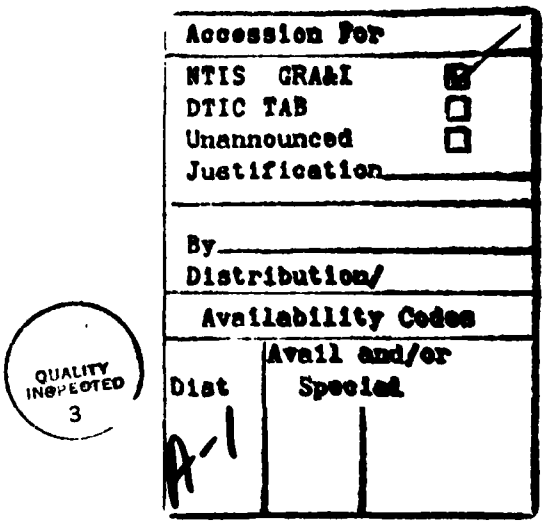

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INTRODUCTION

The objective of this research was to evaluate the effects of two antihistamines on a range of cognitive performances. The evaluation was performed by administering diphenhydramine (Benadryl) or terfenadine (Seldane) to male volunteer subjects prior to their performing on the Naval Medical Research Institute Performance Assessment Battery (NMRIPAB). Diphenhydramine was chosen because of its purported central nervous system (sedative) effects, while terfenadine was chosen because of its purported lack of similar effects.

METHODS

Six males between the ages of 19 and 34 years served as subjects. All sessions were conducted between the hours of 0800 and 1200 while the subjects were alone in a dark room. Medical coverage was available during all experimental sessions. The subjects were compensated for their participation in the study.

The subjects performed on the nine task NMRIPAB (1). The tasks in their order of presentation are enumerated in Figure 1. The PAB was implemented on a microcomputer and required approximately 30 min to complete. The subjects were trained until performance on each task reached a 90% level of accuracy for three consecutive sessions. Between 15 and 22 sessions were

required before this level of accuracy was achieved. Following training, each subject experienced nine experimental sessions during which he was administered either placebo, 60 mg of terfenadine, or 100 mg of diphenhydramine three times each in a mixed order. Drug administrations were spaced at least 48 hours apart.

Drug was administered and sessions occurred at 1 hour, 2 hours, and 3 hours post drug administration. All sessions took place in a quiet room, and the subjects were allowed to read or study between sessions.

RESULTS

Diphenhydramine produced decreases in the accuracy of responding on five of the nine tasks of the NMRIPAB. It also produced increases in response latency in two of the nine tasks. The PAB tasks that proved sensitive to the effects of diphenhydramine are indicated in Figure 1 with an asterisk. Terfenadine did not produce consistent effects on any task.

Two examples of the effects observed are presented in Figures 2 through 4. The effects of diphenhydramine on the accuracy and latency of Repeated Acquisition responding is presented in Figures 2 and 3. In this task the subject must learn a new sequence of responses each session. There are four

available response locations, and each sequence is twelve responses long. At each location in the sequence, only one of the four possible responses is correct. For instance, during one session the correct sequence might be 421324314312, while during the next session it might be 312423414213. Each session consists of 25 completions of the response sequence. These results are contrasted with the findings from the similar Chain Performance task in which the sequence remains the same from session to session. Diphenhydramine produced significant ($p<.05$) increases in the number of errors committed on this task and the duration of sessions during the third hour of testing. No significant changes were observed during the Chain Performance task.

The effects of diphenhydramine on the accuracy and latency of responding during the Grammatical Reasoning task is presented in Figure 4. The subject is presented with statements such as:

A IS FOLLOWED BY B AB, or

A DOES NOT PRECEDE B BA

and is required to respond true or false to the relationship of A and B. Diphenhydramine produced a significant ($p<.05$) increase in response latency during the second hour of PAB testing.

DISCUSSION

Five of the nine tasks comprising the NMRIPAB proved to be sensitive to diphenhydramine but not to terfenadine administration. Measures of accuracy of responding, either percent correct or percent errors, were more frequently affected than response latency or the speed of responding.

The majority of the effects observed during diphenhydramine administration occurred during the second or third hour of testing. This finding is in conformance with the reported pharmacokinetics of diphenhydramine (2). Given orally, this drug reaches maximal concentration in the blood in about two hours and remains at that level for another two hours.

The subjects responded differently to the various PAB tasks and were differentially affected by the drug. This finding reinforces the battery concept of performance assessment (3).

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3. Thorne, D. R., S. G. Genser, H. C. Sing, and F. W. Hegge. The Walter Reed Performance Assessment Battery. In: Neurobehavioral Toxicology and Teratology: Workshop on Neurotoxicity Testing in Human Populations. D. A. Otto and D. Eckerman (Eds), 1985; 7(4):415-418.

FIGURE LEGENDS

Figure 1. A listing of the tasks comprising the NMRIPAB in their order of presentation. Each task was in effect for N trials or X seconds, which ever occurred first.

Figure 2. Total session errors for the three hours of Repeated Acquisition (left) and Chain Performance (right) testing are presented. The data for placebo, terfenadine, and diphenhydramine are represented by the small cross hatched, striped, and large cross hatched columns, respectively. Each column represents the average of three replications for each of six subjects; the error bars represent the standard deviations.

Figure 3. Session duration in seconds for the three hours of Repeated Acquisition (left) and Chain Performance testing are presented. The data for placebo, terfenadine, and diphenhydramine are represented by the small cross hatched, striped, and large cross hatched columns, respectively. Each column represents the average of three replications for each of six subjects; the error bars represent the standard deviations.

Figure 4. Percent errors (left) and response latencies (right) for the three hours of Grammatical Reasoning testing

are presented. The data for placebo, terfenadine, and diphenhydramine are represented by the small cross hatched, striped, and large cross hatched columns, respectively. Each column represents the average of three replications for each of six subjects; the error bars represent the standard deviations.

APPENDIX

NMRIPAB TASKS

STERNBERG

CHAIN PERFORMANCE

* PATTERN COMPARISON
* GRAMMATICAL REASONING
* MATCHING-TO-SAMPLE

VISUAL SCANNING

* MANIKIN
* REPEATED ACQUISITION

STROOP

FIGURE 1

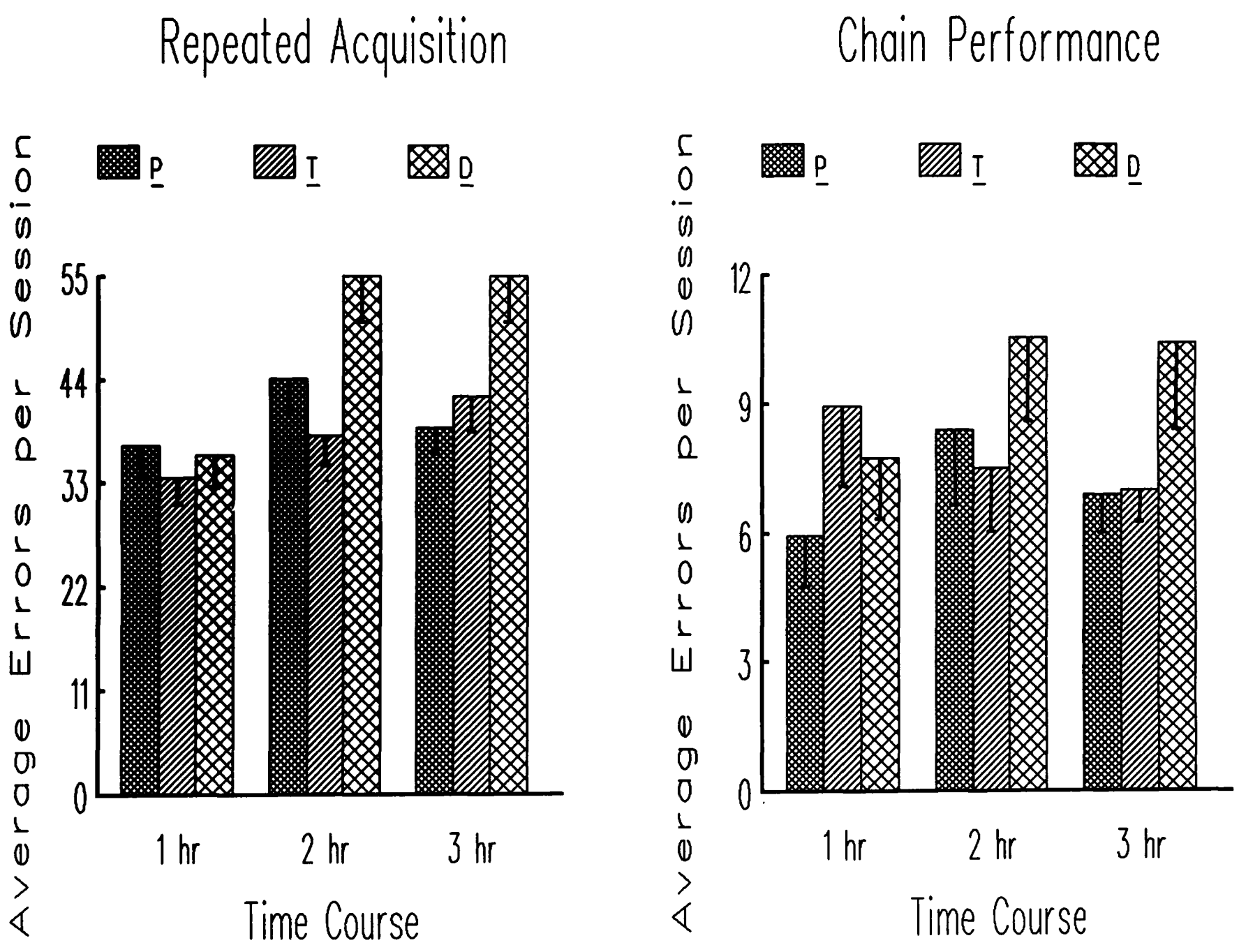
Repeated Acquisition
P
T
D
Average Errors per Session
55
44
33
22
11
0
1 hr
2 hr
3 hr
Time Course
Chain Performance
P
T
D
Average Errors per Session
12
9
6
3
0
1 hr
2 hr
3 hr
Time Course

FIGURE 2

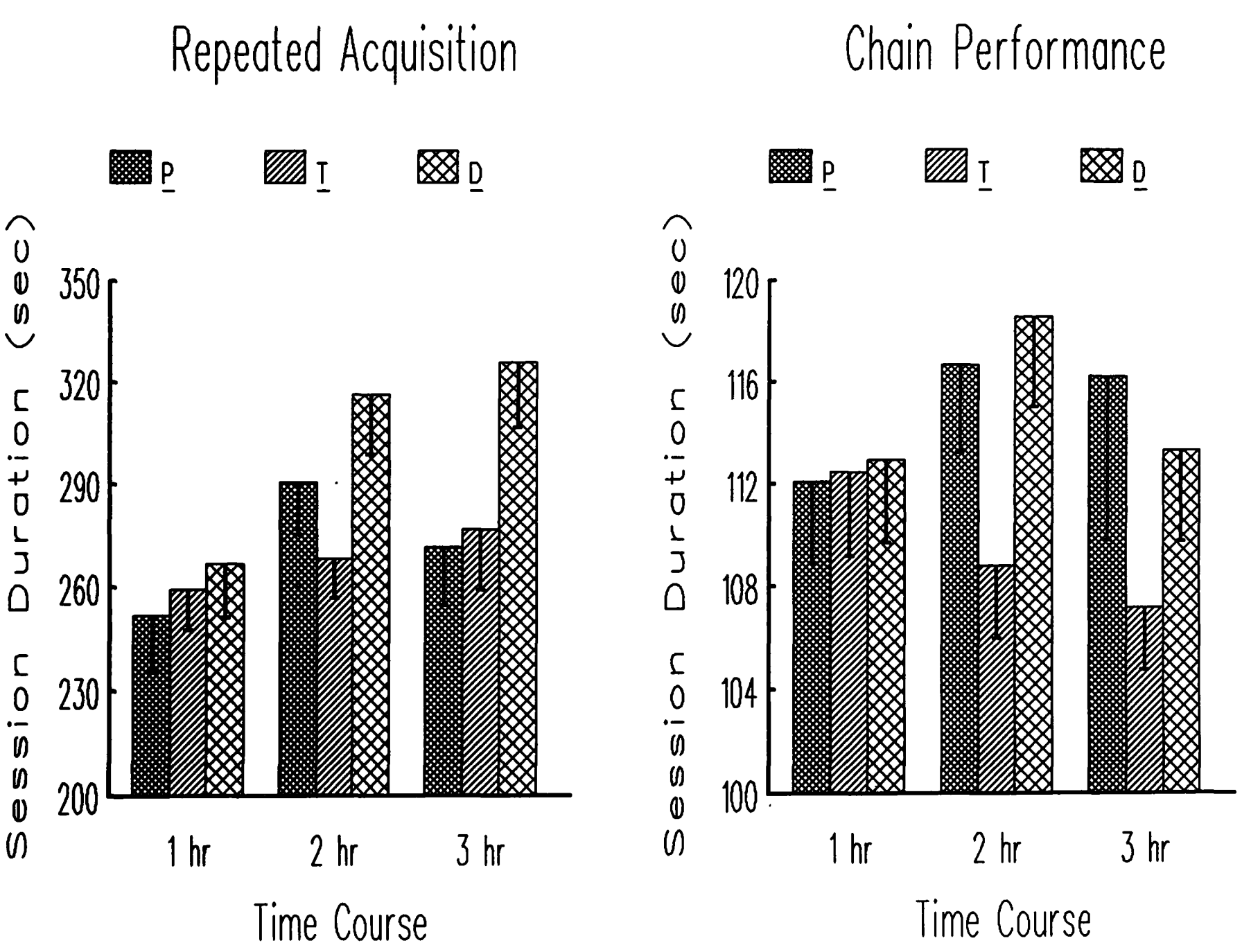
Repeated Acquisition
P
T
D
Session Duration (sec)
350
320
290
260
230
200
1 hr
2 hr
3 hr
Time Course
Chain Performance
P
T
D
Session Duration (sec)
120
116
112
108
104
100
1 hr
2 hr
3 hr
Time Course

FIGURE 3

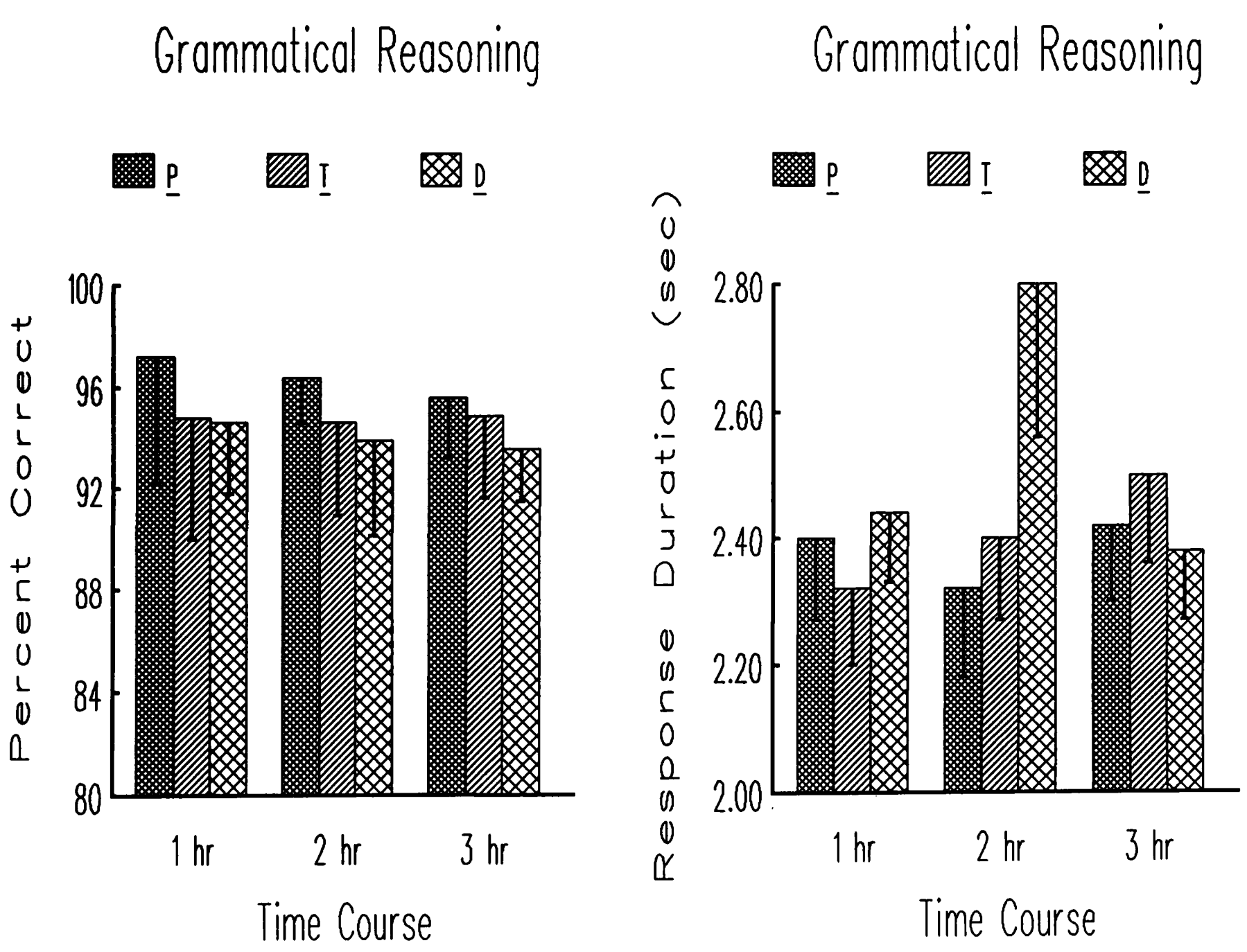
Grammatical Reasoning
P
T
D
Percent Correct
100
96
92
88
84
80
1 hr
2 hr
3 hr
Time Course
Grammatical Reasoning
P
T
D
Response Duration (sec)
2.80
2.60
2.40
2.20
2.00
1 hr
2 hr
3 hr
Time Course

FIGURE 4